

### **Listing of the Claims:**

The following claims replace all prior claim sets of the subject application.

1. (Original) A method for growing islet-producing stem cells (IPSCs), islet progenitor cells (IPCs) and IPC-derived islets (IdIs) comprising the steps of
  - a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby an epithelial monolayer containing IPSCs is produced, and
  - b) initiating cellular differentiation, whereby IPCs and IdIs are produced.
2. (Withdrawn) A cellular composition comprising IPSCs produced according to a method comprising the step of:

culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby a ductal epithelial monolayer containing IPSCs is produced.
3. (Withdrawn) The cellular composition of claim 2 wherein said IPSCs are human.
4. (Withdrawn) A cellular composition comprising islet progenitor cells (IPCs) produced according to a method comprising the steps of:
  - a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby a ductal epithelial monolayer containing IPSCs is produced, and
  - b) initiating cellular differentiation, whereby IPCs are produced.
5. (Withdrawn) The cellular composition of claim 4 wherein said IPCs are human.
6. (Original) An *in vitro* produced IPC-derived islet (IdI) comprising  $\beta$  cells and either  $\alpha$  or PP cells, wherein said  $\beta$  cells are located in the center of the IdI, said  $\alpha$  or PP cells are located in an outer cortex of the IdI, and proliferating and undifferentiated cells are located in an inner cortex of the IdI, wherein about 20 to 25% of the total cells of said IdI are  $\beta$  cells.

7. (Original) An IdI produced according to a method comprising the steps of:
  - a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of IPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby an epithelial monolayer containing IPSCs is produced, and
  - b) initiating cellular differentiation, whereby IPCs and IdIs are produced.
8. (Original) The IdI of claim 7 wherein said IdI is human.
9. (Withdrawn) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises implanting the IPSC composition of claim 2 into a tissue of the mammal.
10. (Withdrawn) The method of claim 9 wherein said IPSCs are encapsulated in an insulin, glucagon and somatostatin permeable capsule.
11. (Withdrawn) The method of claim 10 wherein said capsule comprises hyaluronic acid.
12. (Withdrawn) The method of claim 9 wherein the IPSCs originate from an individual into whom the IPSCs are implanted.
13. (Withdrawn) The method of claim 9 wherein the pancreatic disease is insulin-dependent diabetes.
14. (Withdrawn) A composition comprising the IPSCs of claim 2 wherein the IPSCs are encapsulated in hyaluronic acid.
15. (Withdrawn) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises implanting the IPC of claim 4 into a tissue of the mammal.

16. (Withdrawn) The method of claim 15 wherein the IPCs are encapsulated in an insulin, glucagon and somatostatin permeable capsule.
17. (Withdrawn) The method of claim 16 wherein the capsule is hyaluronic acid.
18. (Withdrawn) The method of claim 15 wherein the IPSCs from which the IPCs arise originate from an individual into whom the IPCs are implanted.
19. (Withdrawn) The method of claim 15 wherein the pancreatic disease is insulin-dependent diabetes.
20. (Withdrawn) A composition comprising the IPCs of claim 4 encapsulated in hyaluronic acid.
21. (Original) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises implanting the IdI of claims 6 or 7 into a tissue of the mammal.
22. (Original) The method of claim 21 wherein the IdI is encapsulated in an insulin, glucagon and somatostatin permeable capsule.
23. (Original) The method of claim 22 wherein the capsule is hyaluronic acid.
24. (Original) The method of claim 21 wherein the IPSCs from which the IdIs arise, originate from an individual into whom the IdI is implanted.
25. (Original) The method of claim 21 wherein the pancreatic disease is insulin-dependent diabetes.
26. (Original) A method of treating pancreatic disease or producing a pancreas-like structure in a mammal which comprises the steps of

a) culturing pancreatic cells from a mammalian species *in vitro* under conditions that are favorable to the survival of iPSCs and ductal epithelial cells, and substantially lethal to differentiated cells, whereby a ductal epithelial monolayer containing iPSCs is produced,

b) initiating cellular differentiation, whereby IPCs and IdIs are produced,

c) implanting in a mammal a composition comprising cells or tissue selected from the group consisting of said ductal epithelium, iPSCs, IPCs, IdIs and any combination thereof, whereby a pancreas-like structure and islet hormones are produced, providing for the treatment of the pancreatic disease.

27. (Original) The method of claim 26 wherein said composition is encapsulated before said implantation step.

28. (Original) The method of claim 26 wherein said implantation step comprises implanting into the mammal=s pancreatic tissue.

29. (Original) The method of claim 26 wherein said implantation step comprises implanting into a subcutaneous pocket of the mammal.

30. (Original) The method of claim 26 wherein said implantation step comprises implanting beneath a kidney capsule in the mammal.

31. (Withdrawn) A composition comprising the iPSCs of claim 2 as modified to substantially reduce expression of an antigen selected from the group consisting of insulin dependent diabetes associated autoantigens, GAD, 64 kD islet cell surface antigen and human leukocyte antigens, whereby IPCs and cells in IdIs arising from said modified iPSCs do not substantially express said antigen.

32. (Withdrawn) A composition comprising the IPCs of claim 4 as modified to substantially reduce expression of an antigen selected from the group consisting of insulin dependent diabetes associated autoantigens, GAD, 64 kD islet cell surface antigen and human leukocyte antigens, whereby cells in IdIs arising from said modified IPCs do not substantially express said antigen.

33. (Original) A method for analyzing the differentiation of pancreatic stem cells which comprises culturing *in vitro* the IPSC composition of claim 2.
34. (Original) The method of claim 33 further comprising the step of inducing said IPSCs to initiate differentiation into IPCs and IdIs, whereby stages of differentiation are identified.
35. (Original) The method of claim 34 further comprising the step of identifying mRNA or protein markers specific to a stage of differentiation.
36. (Original) The method of claim 35 wherein the markers are expressed on the cell surface, are secreted or are intracellular.
37. (Original) An antibody to a marker of claim 36.
38. (Original) A method for long-term propagation of IPSCs which comprises serially transferring a cellular composition comprising material selected from the group consisting of ductal epithelium, IdIs, IPSCs, IPCs and any combination thereof.
39. (Original) The method of claim 38 wherein said serial transfer involves the transfer of IdIs and IPSCs.
40. (Original) A method for inducing neovascularization in a pancreatic implant in a mammal comprising transplanting into said mammal the pancreatic implant comprising cells or tissue selected from the group consisting of IPSCs, IPCs and IdIs, whereby vascularization is induced or enhanced.
41. (Original) The method of claim 40 wherein the implanted tissue is IdIs.

42. (Original) A pancreas-like structure produced by implantation of cells or tissues selected from the group consisting of iPSCs, IPCs and IdIs, comprising at least 50% by weight of endocrine tissue.

43. (Withdrawn) The pancreas-like structure of claim 42 wherein said structure comprises a contiguous mass of endocrine cells having a substantial loss of islet structure.

44. (Original) The pancreas-like structure of claim 42 wherein said structure comprises endocrine cells arranged in IdIs or anatomically similar structures.

45. (Withdrawn) A method of inducing differentiation of cultured iPSCs comprising contacting said iPSCs with a composition selected from the group consisting of serum, extracellular matrix (ECM) and nicotinamide (NAD).